Clinicopathological Spectrum Of Breast Cancer Patients With Reference To Nottingham Prognostic Index

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Abstract: <u>Background & objectives:</u> Breast cancer is one the major causes of cancer related deaths in women worldwide. It has variable clinical, pathological and prognostic determinants. Nottingham modification of Bloom Richardson grading and Nottingham Prognostic Index have significant impact on the prognostication of breast carcinoma. The present study is conducted to evaluate the clinico-pathological features and to study their association with Modified Bloom Richardson grade and Nottingham Prognostic Index in patients attending a Tertiary care hospital in North Karnataka. <u>Methods:</u> Operated specimens of 136 cases of breast carcinoma were evaluated for clinico-pathological features. The association between these variables and Bloom Richardson grades and Nottingham Prognostic Index were calculated using Chi-square test. P value of </=0.05 was considered significant. <u>Results</u>: Size, lymphovascular invasion, necrosis, lymphocytic infiltration showed significant association with higher grades. Menopausal status, Hindu religion, Fixation to chest, lymphovasular invasion, necrosis, lymphnode positivity showed significant association with poor indices of NPI scores. <u>conclusion</u>: Evaluation of the clinicopathological features of breast carcinoma along with modified Bloom Richardson grade and Nottingham prognostic Index may help in planning and making therapeutic decisions in patients with breast carcinoma. [Hungund B Natl J Integr Res Med, 2019; 10(3):20-28]

Key Words: Breast carcinoma , clinical features, Grade, NPI, pathological features

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Introduction: Breast carcinoma is one of the leading causes of malignancy in women globally. The incidence is on the rise worldwide with greatest increase seen in Asian countries. It is the most common cancer in women in urban India and second commonest in rural India1. It is a heterogeneous disease with variable histological, clinical and biological prognostic determinants2. The prognosis depends on number of factors including clinical and pathological features. Though the molecular markers are increasingly being used, the basic clinical and pathological features are the important factors for prognostication of breast cancer especially in developing countries. With increasing urbanization and globalization, there has been changing trend of risk factors and prognostic factors in Indian population3. Hence there is a need to relook into these factors in the local population which will help in assessing the disease burden and its impact on health care of the community and for planning of management strategies and policies.

Nottingham's modification of Bloom Richardson grading involves a semi quantitative evaluation of three morphological variables-the percentage of tubule formation, the degree of nuclear pleomorphism and an accurate mitotic count using a defined field area. An overall grade is derived from summation of individual scores for

variables. the three Three grades of differentiation are used fairly objectively for grading the tumor and proved to be an independent predictor for Breast cancer specific survival (BCSS) and DFS(Disease free survival) 4. Nottingham Prognostic Index(NPI) which uses the grade and clinical parameters like lymph node status and tumor size, can provide simple, inexpensive, accurate and validated method for assessing the patient prognosis5. Hence, this study was undertaken to evaluate the clinical and pathological features of breast carcinoma in the present setting and study the association of these features with Modified Nottingham's Bloom Richardson grade and Nottingham Prognostic Index.

Material and Methods: The study was approved by the Institutional Ethical committee. The present study is a retrospective hospital based study conducted in tertiary health care centre in North Karnataka. The hospital caters to the diverse population from various socioeconomic groups. The study was conducted in the department of Pathology attached to the hospital. The study included all the patients whose operated specimens were received in the Department of pathology attached to the hospital. These cases were evaluated for sociodemographic profile, clinical features, and

pathological features including the gross and microscopic examination findings. The details regarding the socio-demographic factors and clinical features were obtained from medical records department of the hospital. The details of pathological findings were obtained from the department of pathology. The Hematoxylin and Eosin (H and E) stained slides were retrieved from the archives of the department of pathology and reviewed by two pathologists for the microscopic findings. The socio-demographic and clinical details included age, marital status, menopausal status, parity, mode of presentation, duration of lump. Clinico-pathological details included site, side, skin changes, involvement of nipple and areola, type of surgery, size of tumor, involvement of margins, status of lymph nodes, findings microscopic including Nottingham modified Bloom Richardson grade, and Nottingham Prognostic Index . The other microscopic details like histological type, lymph vascular invasion, in-situ changes, fibrosis(elastosis), necrosis, and other specific changes were evaluated. Nottingham prognostic index (NPI) was calculated using three pathological criteria: the size of the lesion; number of involved lymphnodes; and the the grade of the tumor. The index was calculated using the formula: NPI = $[0.2 \times S] + N + G$ where S is the size of the index lesion in centimetres , N is the node status: 0 nodes = 1, 1-4 nodes = 2, >4 nodes = 3 and G is the grade of tumour: Grade I =1, Grade II =2, Grade III =3. The scores were categorized into three prognostic groups with score of <3.4 ,>3.4-5.4, and >5.4 which indicated Excellent/good , moderate and poor prognosis 6 , ⁷.

Statistical Analysis: The distribution of various socio-demographic, clinical and pathological features were expressed in percentages. The averages were calculated wherever relevant.

Chi-square test was used to study the association between the variables. Microsoft-Excel was used for statistical analysis.

Results: A total of 136 patients operated for Breast carcinoma during the period of 5 years (2007 to 2011) were included in the study. The age ranged from 29-83years.The mean age was 51.9 years. Majority (53.7%) of the patients were more than 50 years and majority(63.24%) of them had attained menopause. Majority (86.03%) belonged to Hindu religion. All the patients included were married and were parous. Family history was present in only 2.9% .Lump in breast was the most common presenting symptom and majority(77.2%) presented with symptoms for less than 6months. Majority (86.03%) presented for the first time and only 13.09% cases presented with recurrent symptoms. Skin ulceration, nipple discharge, nipple excoriation and limb edema were few other presenting symptoms. Skin puckering and fixation to chest were present in 36.03% and 13.24% cases respectively. Right and left breast involvement was seen almost with equal frequency and only 2cases (1.47%) showed bilateral involvement. Upper outer guadrant was the most commonly involved guadrant followed by Upper inner, Lower outer, Lower inner, and central. 14% cases showed involvement of more than one quadrant. The samples were obtained mostly by Modified radical mastectomy(72.06%) followed by excisional biopsy, needle biopsy, quadrantectomy with axillary clearance, simple mastectomy with axillary clearance ,simple mastectomy only, partial mastectomy, and lumpectomy with axillary clearance. The size of the tumor ranged from 1cm to 11cm. the mean size was 3.63cm. Majority of the tumors were 2-5cm in size. Infiltrating ductal carcinoma NOS was the most common histological type seen in the study. Infiltrating lobular, mucinous, Medullary, papillary, apocrine were other histological types. Few of them had infiltrating ductal carcinoma along with features of other types. Majority were grade II(58.8%) tumors, followed by grade III and Grade I tumors. Pagetoid change and skin involvement were seen in 2.9% and 11.7% cases. 22.79% of the cases showed involvement of margins. Lymphovascular invasion and necrosis were seen in 56.6% and 55.1% respectively. Fibrosis (desmoplasia), in-situ changes and lymphocytic infiltrate were seen in 83% ,63.9% and 86.03% of the cases respectively. Perineural invasion was seen in 6 (4.41%) cases only. Lymphnodes were retrieved in 107 cases of which 62(57.94%) cases showed positivity. Nottingham prognostic index was calculated in 107 cases and majority belonged to poor prognosis group(34.6%).

Chi square analysis showed statistically significant association of size, lympho- vascular invasion and histopathological type,fixation to chest wall and lymphnode positivity with higher grade of the tumor(Table 1,2). Though not statistically significant it was observed that higher grade tumor were seen in younger age groups ie < 50 years age group and increasing duration of presentation, Statistically significant association was seen between , Hindu religion, fixation to chest wall, lymphovascular invasion , necrosis and lymph node positivity and poor indices of the NPI scores.(Table 4) It was possible to assess Pagetoid change in 111 cases and had no significant association with grade of tumor.(Table 3)

Table 1: Bloom Richard	son Grades of brea	st carcinoma by	clinicopatholog	gical features	;
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	Grade I(%)	GradeII(%	GradeIII(%	Total	p value
	21(15.4)	80(58.8)	35(25.7)	136	
Age					
>50	15(20.5)	41(56.2)	17(23.3)	73	>0.05
<50	6(9.5)	39(61.9)	18(28.6)	63	
Menopausal status					>0.05
Menopause	16(18.6)	53(61.6)	17(19.8)	86	
Premenopausal	5(10)	27(54.0)	18(36)	50	
Duration of lump(months)					>0.05
<6	18(17.1)	61(58.1)	26(24.8)	105	
6-12	2(14.3)	9(64.3)	3(21.4)	14	
12+	1(5.9)	10(58.8)	6(35.3)	17	
Recurrence					
Non-Recurrent	17(14.5)	70(59.8)	30(25.6)	117	
Recurrent	4(21.1)	10(52.6)	5(26.3)	19	
Family history					>0.05
Absent	20(15.2)	79(59.8)	33(25)	132	
Present	1(25.0)	1(25.0)	2(50)	4	
Religion					>0.05
Hindu	18(15.4)	69(59)	30(25.6)	117	
Others	3(15.8)	11(57.9)	5(26.3)	19	
Side					>0.05
Right	11(15.9)	42(60.9)	16(23.2)	69	
Left and Bilateral	10(14.9)	38(56.7)	19(28.4)	67	
Quadrant					>0.05
Lower inner	1(10)	6(60)	3(30)	10	
Lower outer	4(15.4)	13(50.0)	9(34.6)	26	
Upper inner	3(9.7)	19(61.3)	9(29)	31	
Upper outer	9(20.5)	27(61.4)	8(18.2)	44	
Others	4(16)	15(60.0)	6(24)	25	
Histopathological Type					
IDC NOS	11(10.6)	67(64.4)	26(25)	104	
Others	10(31.3)	13(40.6)	9(28.1)	32	
Lymphovascular invasion					<0.01
Absent	16(27.1)	32(54.2)	11(18.6)	59	
Present	5(6.5)	48(62.3)	24(31.2)	77	
Necrosis					>0.05
Absent	14(23.0)	44(72.1)	3(4.9)	61	
Present	7(9.3)	36(48.0)	32(42.7)	75	
Fibrosis					>0.05
Absent	4(17.4)	10(43.5)	9(39.1)	23	
Present	17(15)	70(61.9)	26(23.0)	113	
Fibrocystic change					>0.05
Absent	18(17.6)	58(56.9)	26(25.5)	102	
Present	3(8.8)	22(64.7)	9(26.5)	34	
In-situ					>0.05

NJIRM 2019; Vol.10(3) May-June

Clinicopathological spectrum of breast cancer

Absent	6(12.2)	27(55.1)	16(32.7)	49	
Present	15(17.2)	53(60.9)	19(21.8)	87	
Lymphocytic infiltration					>0.05
Absent	6(31.6)	12(63.2)	1(5.3)	19	
Present	15(12.8)	68(58.1)	34(29.1)	117	
Perineural Invasion					>0.05
Absent	20(15.4)	76(58.5)	34(26.2)	130	
Present	1(16.7)	4(66.7)	1(16.7)	6	
Size(cm)					>0.05
<2	3(42.9)	2(28.6)	2(28.6)	7	
2-5	16(14)	75(65.8)	23(20.2)	114	
>5	2(13.3)	3(20.0)	10(66.7)	15	
Margins					>0.05
Involved	5(16.1)	13(41.9)	13(41.9)	31	
Not involved	12(15.6)	48(62.3)	17(22.1)	77	
Close	1(14.3)	5(71.4)	1(14.3)	7	
Not assessed	3(14.3)	14(66.7)	4(19.1)	21	
Lymphnode					<0.05
Negative	13(28.9)	23(51.1)	9(20)	45	
Positive	6(9.7)	36(58.1)	20(32.3)	62	
Not retrieved	2(6.9)	21(72.4)	6(20.7)	29	

Table 2: Grades of breast carcinoma by fixation chest wall

		-	
Fixation to chest	Grade I&II	GradeIII	Total
Absent	93(78.8)	25(21.2)	118
Present	8(44.4)	10(55.6)	18
Total	101(74.3)	35(25.7)	136

Table 3: Grades of breast carcinoma by Pagetoid change

Pagetoid change	Grade I &II	Grade III	Total	P value
Absent	78(72.9)	29(27.1)	107	>0.05
Present	3(75)	1(25)	4	
Total	81(73)	30(27)	111	

Table 4: Nottingham Prognostic Index by clinicopathological features

	Excellent and good	Moderate	Poor Prognosis(%)	Grand Total	P value
	prognosis (%)	prognosis (%)			
	20(18.7)	50(46.7)	37(34.6)	107	
Age					
>50	15(24.6)	29(47.5)	17(27.9)	61	>0.05
<50	5(10.9)	21(45.7)	20(43.5)	46	
Menopausal status					
Menopause	16(22.5)	36(50.7)	19(26.8)	71	0.9
Premopausal	4(11.1)	14(38.9)	18(50.0)	36	
Duration of lump					
<6months	18(22.2)	36(44.4)	27(33.3)	81	
>6months	2(7.7)	14(53.8)	10(38.5)	26	
Religion					<0.01
Hindu	19(20.2)	41(43.6)	34(36.2)	94	
Others	1(7.7)	9(69.2)	3(23.1)	13	
Skin Puckering					>0.05
Absent	17(24.6)	3246.4 ()	20(29.0)	69	

NJIRM 2019; Vol.10(3) May-June

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Clinicopathological spectrum of breast cancer

Dracont	2(7.0)	10/17 1)	17(447)	20	
Fivetion to Chest	3(7.9)	18(47.4)	1/(44.7)	38	>0.05
Fixation to chest					>0.05
Absent	19(20.4)	45(48.4)	29(31.2)	93	
Present	1(7.1)	5(35.7)	8(57.1)	14	
Quadrant					>0.05
Lower	3(9.4)	18(56.3)	11(34.4)	32	
Upper	14(23.3)	29(48.3)	17(28.3)	60	
Others	3(20)	3(20.0)	9(60)	15	
Histological type					<0.01
IDC NOS	10(12.3)	41(50.6)	30(37.04)	81	
Others	10(37.04)	10(37.04)	7(25.9)	27	
Lymphovascu	lar invasion				
Absent	15(34.1)	23(52.3)	6(13.6)	44	< 0.01
Present	5(7.9)	27(42.9)	31(49.2)	63	
Necrosis					0.025
Absent	12(26.1)	24(52.2)	10(21.7)	46	
Present	8(13.1)	26(42.6)	27(44.3)	61	
Fibrosis					>0.05
Absent	3(16.7)	11(61.1)	4(22.2)	18	
Present	17(19.1)	39(43.8)	33(37.1)	89	
Fibrocystic change					>0.05
Absent	15(18.3)	38(46.3)	29(35.4)	82	
Present	5(20)	12(48.0)	8(32.0)	25	
In-situ changes					>0.05
Absent	5(13.5)	20(54.1)	12(32.4)	37	
Present	15(21.4)	30(42.9)	25(35.7)	70	
Lymphnode positivity					< 0.01
Positive	3(4.8)	24(38.7)	35(56.5)	62	
Negative	17(37.8)	25(55.6)	2(4.4)	45	
Lymphocytic	infiltration				>0.05
Absent	4(33.3)	7(58.3)	1(8.3)	12	
Present	16(16.8)	43(45.3)	36(37.9)	95	

Discussion: Breast carcinoma among women has become the most commonly diagnosed cancer worldwide and second leading cause of cancer related death among women. Despite the current molecular classification of breast carcinoma, the morphological criteria are still widely used in management of breast carcinoma.⁸ It provides an initial approach in the treatment of breast carcinoma. Nottingham's modified Bloom Richardson grading system , when adequately performed provides a simple, inexpensive, accurate and validated method for assessing the prognosis of patients with breast carcinoma and has also been included in the algorithm for defining therapy in patients with breast carcinoma. The robustness of this is further improved by including other parameters like size, lymph node status to give prognostic index called Nottingham Prognostic index(NPI)⁹.

In the present study 136 cases were evaluated for clinical presentation and histopathological features and studied for their relation with grade and Nottingham's prognostic index. The mean age group affected was 51.9 years and majority of them were more than 50 years.

A study conducted in Brazil comparing the morphological aspects according to age also found predominance of women older than 50 years representing 59% of the sample8. They also observed that women > 50 years had more grade III tumors and larger tumors. It was also observed that even among women < 50 years higher grade tumors were more frequent than grade I tumors which is a matter of concern and generates scope for future studies to justify the prevalence ⁸.

Another important factor which was found to be significantly associated with higher grades of tumors were lympho-vascular invasion and lymph node positivity⁸. It has also been observed in literature that regardless of age, axillary lymph node involvement was associated with aggressive grade of the tumor. The overall survival reduces from 75% in node negative tumors to 25-30% in node positive tumors. In the present study also lymphnode positivity was seen in 57.94% cases and was associated with higher grade and NPI scores. In another study conducted in India 78% cases were in age group 40-60 years which is similar to our study where 84% cases were > 40 years. They also observed that majority (82%) were post-menopausal where as in our study 63.2 % were post menopausal¹⁰. Lump was the most common presenting symptom(98.53%).

Symptoms like nipple discharge skin ulceration, nipple excoriation , limb edema were the associated symptoms in 2.9%, 5.88%, 1.47%, 0.74% respectively. Only 2 cases presented with only nipple discharge. Our findings were similar to Pervin et al ¹⁰, with lump as a predominant symptom in 100% cases. However they observed symptoms like pain in 74%, Nipple discharge in 20%, ulceration in 22% cases¹⁰. Right and left breast were involved in almost equal number of cases and only 2cases showed bilaterality, similar to that of Pervin et al ¹⁰. In a study by Kaur M et al¹¹ left breast was more commonly involved (60%) than right(40%) while Saleh F et al ¹² noted a higher proportion of tumours on right side. In another study conducted among Pakistani women it was observed that left breast was more commonly involved than right¹³. However they also observed that Right sided tumors were more aggressive and were associated with higher incidence and earlier occurrence of metastasis as evidenced by positive bone scans. Amer et al ¹⁴ found left breast cancers relatively more than right in all age groups. In the present study there was no significant association of laterality with grade and NPI scores. Upper quadrant (55%)was more commonly involved as compared to lower quadrant.(27%) more so the upper outer quadrant(32.35%) . Pervin et al¹⁰ also observed that 66% showed upper guadrant involvement with predominant involvement of upper outer quadrant (42%). The higher proportion of upper outer quadrant breast carcinomas reflect the greater amount of breast tissue in this quadrant¹⁵. There was no significant association between the side and quadrant involvement with

grade or prognostic score. However study by Deo et al observed that higher risk was associated with tumors located in inner quadrants and periareolar regions. This outcome was however observed in high risk groups and with those treated with conservative therapy.¹⁶

Size of the tumor is an important prognostic factor in the evaluation of breast carcinoma. In the present study the size of the tumor ranged between 1 cm to 11cm. The mean tumor size was 3.64cmwith SD 1.72cm. Majority were 2-5cm (T2) in size.11%were >5cm and only 5.1% were less than 2cm. The size of the tumor showed significant association with the grade and NPI score. The study done in Kolkata ¹⁷ also observed similar finding and higher proportion of tumors in 2-5cm group. However a western study revealed the tumor size of <2cm .This finding cautions us about the fact that there's still lack of awareness among our women about breast cancer and stresses the importance of regular selfexamination of the breast and other screening techniques for early detection of breast carcinoma in India and other eastern countries.

The most common histological type we observed was infiltrating duct carcinoma - NOS which is the most common type observed in literature 8,¹⁹. Though significant association was not observed between the grade, NPI score with histological types, it was observed that majority of medullary (2/2) and papillary carcinoma (3/4) were grade III, while mucinous carcinoma were grade I. Among IDC – NOS majority were grade II tumours(67%). A large population based study from the 11 cancer registries in US it was observed that mucinous and papillary carcinomas occurred in older women while the medullary carcinoma occurred at a young age. Variations in Ethnic /racial compositions were also seen.20 WHO mentions atleast ¹⁷ histological subtypes of breast carcinoma. A review on histological subtypes describes that the pattern of growth of tumors is consistently associated with distinctive clinical presentations and outcome; e.g. tubular carcinoma are associated with almost normal survival. Though higher grade tumors usually have poor prognosis, medullary carcinoma though high grade has relatively good prognosis. Due to relative rarity of the special types, information about the biology and clinical behavior is rarely taken in to account for therapeutic decisions. ²¹

Tumor grade provides an important prognostic information in breast carcinoma. Nottingham modification of Bloom Richardson grading is a time tested tool which has been used regularly in providing prognostic information in breast carcinoma. It has shown to be strongly associated with breast cancer specific survival (BCSS) and disease free survival (DFS) and acts as an independent predictor of both BCSS and DFS4.In the present study it was observed that majority of the cases were grade II tumors (58.82%). Grade I and grade III tumors comprised 15.4% and 25.7% respectively. A histopathological study of breast neoplasms noted that among malignant neoplasms 58% were grade II lesion, 33% were grade I and 9% grade III tumors20. Many of the Indian studies show similar findings 22,²³. However Ghosh et al in their retrospective analysis noted more number of grade III tumors $(75.4\%)^{24}$.

Pagetoid change was observed in only 2.9% cases only .Skin involvement was observed in 11.7%. A study conducted in Kolkata observed skin and nipple areola involvement in 15% cases¹⁷. Involvement of margins especially deeper surgical margin was noted in 22.7% and the tumour was close to the margin in 5.15%. Hamza et al observed surgical margins to be positive in 25.3%25.Adequate surgical margins in breastconserving surgery are an important predictor of local recurrence rates ²⁶. Fixation to chest wall was seen in 13.24% cases and seen more frequently in Grade III tumors (p<0.01). However there was no significant correlation between of chest wall fixation and NPI.

Not many studies have discussed about perineural invasion in breast carcinoma. Perineural invasion (PNI) was said to be positive when tumor cells were seen in the perineurium or the neural fascicles. PNI was present in only 6cases(4.41%) and there was no significant correlation with grade or NPI.A previous study assessing the prognostic value of PNI in breast cancer noted perineural invasion in 25.7% cases ²⁷. PNI positivity was seen13.9% in T1 tumors and 69.7% in T4 tumors (P<0.001). The incidence of PNI was higher in ductal and mixed type carcinomas than in other histologic types (P=0.013). Vascular invasion, axillary lymph node and progesterone receptor positivity ratios were significantly higher in PNI-positive patients than in PNI-negative ones. (P<0.001, P=0.001 and 0.006, respectively). However the study did not

find any difference between PNI-positive and negative patients regarding DFS. Hence they proposed that perineural invasion had no prognostic importance²⁷. However there were only small number of PNI positive cases. More studies need to be considered for making clinical decisions regarding the same.

A large study by National Surgical adjuvant Breast and Bowel project studied the relation between the number of lymph nodes positivity with disease free survival. They observed that the DFS of lymph node negative cases was 85%, with single lymphnode positive cases was 63% and worse prognosis with greater number of nodes. They validated the grouping of breast cancer patients in to negative, 1-3,>/=4 positive nodes28. In the present study of the 107 cases in which lymphnodes were retrieved, 57.9 % showed lymph node positivity. Majoritity showed 1-5 lymphnodes. Also there was significant correlation with grade and NPI. Kwtra et al and Shat e al noted almost similar finding with lymphnode positivity in 48% cases, and 30% of them having up to 3 lymphnodes 5,17.A study conducted in Tamil nadu observed lymph node positivity in 90% cases which is quite high²⁹. It might be due to the setting of the study in Govt. medical College which usually caters to lower socio-economic strata people who are more likely to seek medical attention in late stages . A study on Sudanese population also showed similar results with lymph node positivity in 94.5% and majority (50.9%) showing > 4 axillary lymph nodes25.

Vascular invasion and lymphatic invasion are strongly associated with lymphnode positivity, increasing tumour size, histological grade and type of tumor,. Also vascular invasion has been proved to be an independent prognostic marker for survival and local reccurence 30,31. Hamza et al noted lymphovascular invasion in 38.8% cases (n=33) while Saha et al observed in 25.8%. In the present study it was seen in 56.62% and it was significantly associated with higher grade and poor NPI score ²⁵. Tumor necrosis was defined as confluent cell death in invasive areas of primary cancers. A study conducted by Eastern Cooperative oncology group suggested that confluent tumor necrosis of any dimension in invasive breast cancer in lymphnode positive breast cancer is an independent predictor of early reccurrence and death from disease ³². In the present study also tumor necrosis was

NJIRM 2019; Vol.10(3) May-June

observed in 55.15% and was significantly associated with higher grade and high NPI scores. NPI has been widely adopted as a prognostic tool in breast cancer. Its utility in predicting the outcome in treated patients with breast carcinoma have been shown in various studies. It has been correlated tumor size, grade, lymph node stage and patent survival5. A study conducted in a Govt cancer hospital in Tamilnadu noted that 50% of their cases were in moderate prognosis group (NPI score 3.4-5.4) and 30 % in the Poor prognosis group (NPI score of >5.4).²⁹ Another Indian study conducted in tertiary care center also noted that majority of the patients(56%) had NPI scores of 3.4-5.4 and 34% had >5.45. However a study in Sudanese population noted a predominance of poor prognosis group (48%) similar to the large study with long term follow $up(50\%)^{25}$. In the present study NPI was calculated in 107 cases and there was predominance of patients with moderate prognosis (48.29%) followed by poor prognosis (34.58%). There was also significant correlation between NPI score, other histological parameters like size, lympho- vascular invasion, necrosis and lymphocytic infiltration with higher grade of the tumor. Again this underscores the importance of late presentation in our community and measures to be considered for early detection of breast carcinoma.

Conclusion: Breast carcinoma presents with varied clinical and pathological features. Some of these have significant association with various prognostic fetaures like grades and Nottingham prognostic index. Thus, the optimal use of grading system and Nottingham Prognostic Index along with other parameters can be useful to get useful prognostic information in patients with breast carcinoma and help in therapeutic decisions and counselling.

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References:

1. Dogra A, Doval DC, Sardana M, Chedi SK, Mehta A. Clinicopathological Characteristics of Triple Negative Breast cancer at a tertiary care hospital in India.Asian Pacific Journal of Cancer Prevention 2014;15:10577-83

- Weigelt B, Geyer FC, Reis –Felho JS.Histological types of breast cancer: how special are they?Molecular oncology 2010;4:192-208.
- Khokar A. Breast cancer in India: Where do we stand and where do we go?Asian Pacific Journal of Cancer Prevention; 2012:13(10):4861-66
- 4. Rakha EA, El-Syed ME,Lee AHS,Elston CW, Grainage MJ, Hodi Z, Blamey RW, Ellis IO. Prognostic Significance of Nottingham Histologic grade in breast invasive carcinoma.Journal of Clinical oncology 2008;26(19):3153-8.
- Kwatra A, Aggarwal D,Gupta R, Chaturvedi AK, Kudesia M,Singh S.Correlation of various histopathological prognostic factors with Nottinham prognostic index and microvessel density in invasive breast carcinoma:A study of 100 cases.Indian J cancer 2015;52:110-3)
- Galea MH, Blamey RW, Elston CE, Ellis IO. The Nottingham Prognostic Index in primary breast cancer. Breast Cancer Research & Treatment 1992;22(3):207-19
- Blamey RW, Ellis IO, Pinder SE, Lee AH, 7. Macmillan RD, Morgan DA, et alSurvival of invasive breast canceraccording to Nottingham prognostic index in cases diagnosed in 1990-1999. Eur Cancer.2007;43(10):1548-55
- Aquino RPF,Pinheiro LGP,Ferreira MVP, cavecante DIM,Oliviera ALS, Gomes NN etal Ducatal carcinoma of the breast:Morphological aspects according to age. J Bras Patol Med 2015;51(4):252-7.
- Rakha EA, Reis-Filho JS, Baehner F, Dabb DJ, Decker T, Eusebi V et al. breast cancer prognostic classification in the molecular era: The role of histological grade. Breast cancer research 2010;12:207)
- Pervin MM, Nath HD,Bahar MM,Alam A, Bhowmik J.Study o clinical presentation of breast carcinoma of 50 cases.Chattagram Maa-O-Shishu Hospital Medical College Journal 2013;13(2):8-11
- Kaur M,Kaur H,Manjari M, Rai V, Kaur K. Assessment of Clinical parameters and histopathological gradingof breast cancer. International Journal of Contemporary Medical Research 2016;3(10):2938-41) I
- 12. Saleh F, Abeen S. Pathobiological features of Breast tumours in state of Kuwait: A comprehensive analysis.J Carcinog.2007;6:12

- Fatima N, Zaman MU, Maqbool A, Khan RH, Riaz N.Lower incidence but more aggressive behaviourof rightsided breast cancer in Pakistani women: does right deserve more respect?Asian Pac J Cancer Prev.2013;14:43-5
- 14. Amer MH . Genetic factors and breast cancer laterality.Cancer Manag Res.2014;6:191-203
- Lee AH. Why carcinoma of breast is more frequent in upper outer quadrants?A case series based on needle core biopsy diagnosis. Breast 2005;14(2):151-2
- Deo V, Dhir M, Gupta SD, Hazrah P, Parshad R. Prognostic significance of location of Primary Tumor in operable breast cancers.Indian journal of cancer.2009:46(2):139-45.)
- Saha K, Raychaudhuri G, Chattopadhyay BK. Clinico-pathological study of breast carcinoma: A prospective two-year study in a tertiary care hospital. Clin Cancer Investig J 2013;2:34-40
- Taucher S, Rudas M, Mader RM, Gnant M, Dubsky P, Bachleitner T. Do we need Her -2/ neu testing for all patients with primary Breast carcinoma?. Cance 2003;98:547-53
- Mudholkar VG, Kawade SB, Mashal SN . Histopathological Study of neoplastic lesions of Breast.Indian medical Gazette.2012;353-64
- 20. .Li CI, Uribe DJ, Daling JR. Clinical characteristics of different histological types of breast cancer. British Journal of cancer2005;93:1046-1052.
- 21. Weigelt B, Geyer CG, Reis- Filho JS.Histological types of breast cancer: How special are they?Molecular Oncology 2010;4(2):192-208)
- 22. Bhagat VM,Jha BM,Patel PR.correlation of hormonal receptor and Her-2/neuexpressio in brest cancer:Astudy at a tertiary care hospital in South Gujarath.National Journal of medical Research2012;2(3):295-8
- 23. Geetamala K, Murthy Srinivas, Vani BR, Rao S.Histopathological grade versus hormone receptor status in Breast carcinoma_treasure the past.Internatinal Journal of biomedical research.2015,;6(7):466-71.
- 24. Ghosh J, Gupta S, Desai S, Shet T, Radhakrishnan S, Suryavanshi P, Parmar V, Jalali R, Goyal G, Hawaldar R, Patil A, Nair N, Badwe R A. Estrogen, progesterone and HER2 receptor expression in breast tumors of patients, and their usage of HER2-targeted

therapy, in a tertiary care centre in India. Indian J Cancer 2011;48:391-6

- 25. Hamza AA, Idris SA, Al-haj MB, Mohammed AA. Prognostication of breast cancer using Nottingham Prognostic Index in Sudanese patients. International Journal of Public health Research 2014;2(1):1-5
- 26. Revez E, Khan SA.What Are Safe Margins of Resection for Invasive and In Situ Breast Cancer?Oncology2011.url <u>www.cancernetwork.com/.../what-are-safe-</u> <u>margins-resection-invasive-and-situ-breast</u>
- 27. Duraker N, Cayanak ZC, Turkoz K. Perineural invasion has no prognostic value in breast carcinoma. The Breast.2006; 15(5):629-34
- 28. Fisher B, Bauer M, Wickerman DL, Redmond CK, Fisher ER, Cruz AB et al . Relation of number of positive axillary nodes to the prognosis of patients with breast cancer. An NSABP update. Cancer 1983;52:1551-7.
- 29. Sivakumar S, Devraj SN. Histopathology of breast cancer patients in Tamilnadu: Tumor grading and staging through NPI. Journal of Pharmacy Research 2011;4(10):3635-37
- Pinder SE, Ellis IO,Galea M, O'Rouke S, Blamey RW, Elston CW. Pathological Prognostic factors in breast cancer .III. vascular Invasion: Relationship with reccurenceand survival in a large study with long term follow up. Histopathology. 1994;24:41-7
- 31. Lauria R,Perrone F, Carlomagno C, De Lauraentis M, Morabito A, Gallo C et al The prognostic value of lymphatic and blood vessel invasion in in operable breast cancer. Cancer 1995;76:1772-8
- 32. Gilchrist KW, Gray R, Fowble B, Torney DC, Taylor SG 4th.Tumor necrosis is a prognostic predictor for early recurrence and death in lymph node-positive breast cancer: a 10-year follow-up study of 728 Eastern Cooperative Oncology Group patients. Journal of Clinical Oncology 1993 11:10, 1929-1935

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